Hon. Commissioner of Patents and Trademarks

S/N 09/712,364

Atty ABH

Re: Applicant - Lange et al

Case No. 93,473-G

Method And Composition For Inhibiting Cholesterol Esterase

Sir:

Please place the Patent Office receipt stamp hereon and mail to acknowledge receipt of:

- ☒ Transmittal Letter
- ☒ Petition for Two Month Extension of Time
- ☒ Reply to March 22, 2002 Official Action with Marked Up Copy of Claims and Clean Copy of Claims
- ☒ Filing Fee Check
- ☐ Other

MAILED: 8/21/02

Fee Enclosed

$ 200.00

Respectfully,
McDonnell Boehnen Hulbert & Berghoff
Attorney for Applicant

mbhb

McDonnell Boehnen Hulbert & Berghoff
Law Offices

300 South Wacker Drive
Chicago, Illinois 60606-6709
www.mbhb.com

312 913 0001 phone
312 913 0002 fax

control #
38382

№ 38382

VOUCHER #	INVOICE #	DATE	INVOICE AMT	DESCRIPTION	AMOUNT PAID
101260	40.253 Judy J	08/21/2002	200.00		200.00

Vendor ID: AS0802 Vendor Name: Commissioner for Patents Check Date: 08/21/2002 TOTAL CHECK: 200.00

THE FACE OF THIS CHECK IS PRINTED BLUE - THE BACK CONTAINS A SIMULATED WATERMARK

mbhb

McDonnell Boehnen Hulbert & Berghoff
Law Offices
300 South Wacker Drive
Chicago, Illinois 60606-6709
www.mbhb.com

USBANK
70-477-719

№ 38382

CHECK NO.	CHECK DATE	VENDOR NO.
38382	08/21/2002	AS0802

PAY TWO HUNDRED AND 00/100 Dollars

CHECK AMOUNT
$*** *** *** 200.00

TO THE ORDER OF

Commissioner for Patents

John F. Hoffman

MP

⑈038382⑈ ⑆071904779⑆ 41707962 9⑈

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 93,473-G)

In re Application of:	)	
	)	Examiner: L.C. Maier
Louis G. Lange, et al	)	
	)	
Serial No.: 09/712,364	)	Group Art Unit: 1623
	)	
	)	
Filed: November 14, 2000	)	
	)	
For: Method and Composition for Inhibiting Cholesterol Esterase	)	

TRANSMITTAL LETTER

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In regard to the above identified application,

1. We are transmitting herewith the attached:

   a) Reply to the March 22, 2002 Official Action with Marked Up Copy of Claims and Clean Copy of Claims;
   b) Petition for Two Month Extension of Time; and
   c) Postcard.

2. With respect to fees:

   a. X Attached is a check in the amount of $ 200.00

3. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Commissioner for Patents, Washington, D.C. 20231 on this 21st day of August, 2002.

Respectfully submitted,

A. Blair Hughes
Registration No. 32,901

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive, 32nd Floor
Chicago, IL 60606
(312)913-0001

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

ADDRESS TO:	Attorney Docket No.: 93,473-G
Commissioner for Patents	Application No.: 09/712,364
Washington, D.C. 20231	Filing Date: November 14, 2000
	First Named Inventor: Lange
	Group Art Unit: 1623
	Examiner: Maier

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application to and including August 22, 2002.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

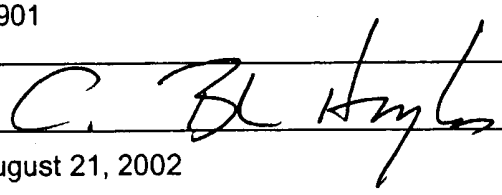
☐ One Month (37 CFR 1.17(a)(1))	$
☒ Two Months (37 CFR 1.17(a)(2))	$400.00
☐ Three Months (37 CFR 1.17(a)(3))	$
☐ Four Months (37 CFR 1.17(a)(4))	$
☐ Five Months (37 CFR 1.17(a)(5))	$

☒ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $ 200.00.

☒ A check in the amount of the fee is enclosed.

☒ The Commissioner is hereby authorized to charge any fees which may be required or to credit any overpayment to Deposit Account Number 13-2490. I have enclosed a duplicate copy of this sheet.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name	A. Blair Hughes
Reg. No.	32,901
Signature	
Date	August 21, 2002

EXT (Rev. 1/3/01)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

(Case No. 93,473-G)

In the Application of:	Louis G. Lange, III, et al.	)	
Serial No.	09/712,364	)	Examiner: L. C. Maier
Filed:	November 14, 2000	)	Group Art Unit: 1623
Title:	Method and Composition for	)	
	Inhibiting Cholesterol Esterase	)	
		)	

Commissioner for Patents
Washington, D.C. 20231

REPLY TO THE March 22, 2002 OFFICIAL ACTION

Dear Sir:

This reply is responsive to the Official Action dated March 22, 2002 (paper no. 8). This response is being submitted during the 2-month extended response period. A request for 2-month extension of time is being submitted with this response.

Claims 12-17 are pending in this Application. Applicants traverse the rejections presented by the Examiner and present the following arguments and amendments.

IN THE SPECIFICATION:

On filing this continuation application a reference to priority was inserted before the first line of the specification. That reference to priority should be cancelled from the specification and replaced with the following priority claim:

This is a continuation application of co-pending application Serial No. 08/816,823 filed on March 17, 1997, which is a continuation of application Serial No. 08/451,563, filed May 26, 1995, now abandoned which is a divisional of application Serial No. 08/322,782 filed on October 13, 1994, now U.S. Patent No. 5,521,303.

IN THE CLAIMS:

Please amend claim 12, as follows:

12. [Once Amended] A method for lowering serum cholesterol in humans comprising administering to a human the combination of an essentially non-absorbable very high molecular weight sulfated polysaccharide having less than about 5.0 wt. percent of sulfated polysaccharides having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate and a second compound that reduces serum cholesterol levels.

Please add claim 17, as follows:

17. [New] A method for lowering serum cholesterol in humans comprising administering to a human the combination of an essentially non-absorbable very high molecular weight sulfated cellulose having less than about 5.0 wt. percent of sulfated cellulose having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate and lovastatin.

Enclosed with this response is a copy of the pending claims marked up to show the above amendments. Also enclosed is a clean copy of the amended claims.

REMARKS

In this response Applicants have amended claim 12, and added new claim 17. No new matter has been added to the Application by way of any of the amendments to the claims. While not necessarily in agreement with the rejections made by the Examiner, Applicants have amended the claims to expedite review and allowance. Applicants also reserve the right to prosecute the canceled claim matter in later applications.

Applicants have added new Claim 17 to further clarify the present invention.

1. **Priority Claim**

The Examiner has pointed out that the U.S. Patent No. listed in the Utility Patent Application Transmittal Sheet for the subject Application contained an incorrect Patent Number. The U.S. Patent No. for the priority claim inserted as the first sentence of the specification has been corrected from 5,521,003 to 5,521,303.

2. **Rejection of Claim 12 under 35 U.S.C. § 102 (b)**

The Examiner has rejected Claim 12 as being anticipated by Howard (US 3,846,541), stating that HOWARD discloses combination drug therapy, comprising ethyl-p-chlorophenoxyisobutyrate or the acid and (1) DEAE Sephadex, (2) cholestyramine, or (3) cholestipol to reduce serum cholesterol in humand with hyperlipidemia. The Examiner pointed specifically to Tables I and II and Tests 1 and 2 in HOWARD.

While not necessarily in agreement with the rejections made by the Examiner, Applicants have amended Claim 12 to expedite review and allowance, while reserving the right to prosecute the canceled subject matter in later applications.

Applicants have amended Claim 12 to recite sulfated polysaccharides having less than about 5.0 wt percent of sulfated polysaccharides having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate. Since sulfated polysaccharides having this molecular weight are not ethyl-p-chlorophenoxyisobutyrate or the acid, Applicants believe that the Examiner's rejection of Claim 12 has been overcome.

3. **Rejection of Claims 12-14 under 35 U.S.C. § 102 (b)**

The Examiner has rejected Claims 12-14 as being anticipated by EAST et al (Annual Inst. Med, 1988), stating that EAST discloses combination drug therapy, comprising lovastatin and gemfibrozil, to reduce serum cholesterol in humans with hyperlipidemia. The Examiner specifically pointed out page 25, left-hand column and Tables 2 and 3.

While not necessarily in agreement with the rejections made by the Examiner, Applicants have amended Claim 12 to expedite review and allowance, while reserving the right to prosecute the canceled subject matter in later applications.

Applicants have amended Claim 12 to recite sulfated polysaccharides having less than about 5.0 wt percent of sulfated polysaccharides having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate. Since sulfated polysaccharides having this molecular weight are not gemfibrozil, Applicants believe that the Examiner's rejection of Claim 12 has been overcome.

Claims 13 and 14 are dependent, directly or indirectly, on Claim 12. As such these dependent claims contain all of the limitations of the independent claim. For this reason Applicants believe that the Examiner's rejection of Claims 13 and 14 has been overcome.

4. **Rejection of Claims 12 and 15 under 35 U.S.C. § 103 (a)**

The Examiner has rejected Claims 12 and 15 as being unpatentable over KRAUSE (US 4,859,703), stating that the claims are drawn to a method for lowering serum cholesterol in humans comprising administration of a first compound that reduces serum cholesterol and a second compound that reduces serum cholesterol, wherein the second compound is an ACAT inhibitor. The Examiner points out that KRAUSE teaches a single dose combination of one of a number of hypocholestemic agents and an ACAT inhibitor. The Examiner further points out that KRAUSE does not specifically exemplify the administration of the compositions to humans to lower serum cholesterol. Finally, the Examiner states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to administer the composition, comprising an ACAT inhibitor and another hypocholestemic agent. The Examiner states that the ordinarily skilled practitioner would be motivated to achieve a lowering of serum cholesterol with a reasonable expectation of success.

Applicants respectfully point out that Claim 12 recites sulfated polysaccharides with a given molecular weight. KRAUSE does not teach sulfated compounds as compounds to lower serum cholesterol. In addition, KRAUSE does not teach sulfated polysaccharides having less than about 5.0 wt percent of sulfated polysaccharides having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate.

Applicants also respectfully point out that there is nothing in KRAUSE that would motivate a person of ordinary skill to go from KRAUSE to the sulfated polysaccharides

of the present application and expect to have a reasonable expectation of success. KRAUSE teaches gemfibrozil, clofibrate, benafibrate, and fenofibrate as the first compound in a combination. If one looks at the compounds listed in KRAUSE one will see that they are all fibric acid derivatives. Fibric acid derivatives are not sulfated polysaccharides. Applicants respectfully point out that there is no motivation in KRAUSE to go from fibric acid derivatives to sulfated polysaccharides. There is no teaching in KRAUSE that would lead a person from KRAUSE to the compounds of the present invention. Also, since the KRAUSE compounds are very different from the compounds of the present invention, there is no reasonable expectation of success in going from fibric acid derivatives to sulfated polysaccharides.

The Examiner has also rejected Claim 15 as being obvious in view of KRAUSE. Claim 15 is dependent on Claim 12. This dependent claim contains all of the limitations of the independent claim.

For these reasons, Applicants respectfully request the Examiner to reconsider the obviousness rejection of Claims 12 and 15.

5. **Rejection of Claims 12-16 under 35 U.S.C. § 103 (a)**

The Examiner rejected claims 12-16 as being unpatentable over LANGE, stating that LANGE teaches the administration of sulfated polysaccharides which act as inhibitors of human cholesterol esterase to lower serum cholesterol. The Examiner points out the abstract, page 5 and example 4 of LANGE, and states that the reference further suggests the use of said polysaccharides in combination with other agents having cholesterol lowering activity. Particular agents pointed out by the Examiner are ACAT inhibitors (page 14, lines 19-25) and lovastatin (page 15, lines 21-24). The Examiner further points out that the use of the polysaccharides in combination with other agents is not specifically exemplified. In addition, the Examiner states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have used the disclosed inhibitors of human cholesterol esterase, the sulfated polysaccharides taught in LANGE in combination with other agents, such as ACAT inhibitors or lovastatin. Further, the Examiner states that the ordinarily skilled practitioner would have been motivated to obtain the combined effect of the agents in lowering serum cholesterol with a reasonable expectation of success.

Applicants respectfully point out that although LANGE teaches very large sulfated polysaccharides of molecular weight greater than 100,000 (see page 9, lines 21-23), LANGE does not teach the need for purified sulfated polysaccharides. On page 9, lines 1-5, of the subject application Applicants teach that the presence of free sulfate and low molecular weight sulfated polysaccharides are undesirable, even toxic. The presence of these impurities makes high molecular weight sulfated polysaccharides unsuitable for human pharmaceutical use. Claim 12 of the present invention contains limitations on the presence of both inorganic sulfate and low molecular weight sulfated polysaccharides.

Applicants further point out that since LANGE did not recognize that purified sulfated polysaccharides containing less than 5 weight percent of sulfated polysaccharides having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate are necessary for human pharmaceutical use, there is no motivation in LANGE to prepare the purified sulfated polysaccharides of the present invention.

The Examiner has also rejected dependent Claims 13-16. Applicants respectfully point out that Claims 13-16 are dependent claims that are subject to all of the limitations of independent Claim 12.

For the above reasons, Applicants ask that the Examiner reconsider the rejection of Claims 12-16 in view of LANGE.

Applicants request the Examiner to reconsider the rejections in view of the above arguments and claim amendments. Favorable reconsideration and allowance of the pending application claims is therefore courteously solicited.

Respectfully submitted,

McDonnell Boehnen
Hulbert & Berghoff

Dated: August 21, 2002

By: C. Blair Hughes

A. Blair Hughes
Reg. No. 32,901
312-913-2123

US Patent Application Serial No. 09/712,364
Marked Up Copy of Pending Claims
Attorney Docket No. 93,473 G
Response to Paper No. 8

12. [Once Amended] A method for lowering serum cholesterol in humans comprising administering to a human the combination of ~~a first compound that reduces serum cholesterol levels~~ an essentially non-absorbable very high molecular weight sulfated polysaccharide having less than about 5.0 wt. percent of sulfated polysaccharides having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate and a second compound that reduces serum cholesterol levels.

13. The method of claim 12 wherein the second compound is at least one cholesterol synthesis blocker.

14. The method of claim 13 wherein the cholesterol synthesis blocker is lovastatin.

15. The method of claim 12 wherein the second compound is an inhibitor of ACAT.

16. The method of claim 12 wherein the sulfated polysaccharide is sulfated cellulose.

17. [New] A method for lowering serum cholesterol in humans comprising administering to a human the combination of an essentially non-absorbable very high molecular weight sulfated cellulose having less than about 5.0 wt. percent of sulfated cellulose having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate and lovastatin.

12. A method for lowering serum cholesterol in humans comprising administering to a human the combination of an essentially non-absorbable very high molecular weight sulfated polysaccharide having less than about 5.0 wt. percent of sulfated polysaccharides having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate and a second compound that reduces serum cholesterol levels.

13. The method of claim 12 wherein the second compound is at least one cholesterol synthesis blocker.

14. The method of claim 13 wherein the cholesterol synthesis blocker is lovastatin.

15. The method of claim 12 wherein the second compound is an inhibitor of ACAT.

16. The method of claim 12 wherein the sulfated polysaccharide is sulfated cellulose.

17. A method for lowering serum cholesterol in humans comprising administering to a human the combination of an essentially non-absorbable very high molecular weight sulfated cellulose having less than about 5.0 wt. percent of sulfated cellulose having a molecular weight less than 75,000 Daltons and containing less than 0.5 weight percent of inorganic sulfate and lovastatin.